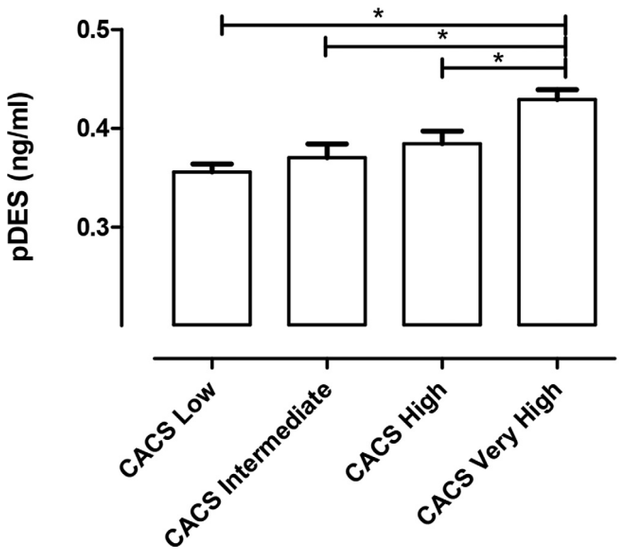

Abstract S51 Figure 1 Differences in pDES between patients with very high CACS and lower CACS levels (* $p < 0.01$)

Introduction COPD is a risk factor for cardiovascular comorbidities. Elastin degradation represents a shared mechanism for the pulmonary and vascular features.

Methods and Results Plasma desmosine (pDES), a marker of elastin degradation, was measured in 955 COPD patients (609 male, age 63.1 ± 7.2 years, FEV_1 50.6 ± 15.1%predicted) by an isotope dilution LC-MS/MS method. Coronary artery calcification (CACS), a surrogate of atherosclerosis, was assessed in 440 standard CT scan images (low 1000 AU).

Results pDES was elevated in patients with cardiovascular comorbidities ($p < 0.01$) and correlated with FEV_1 ($r = 0.39$, $p < 0.0001$), MMRC ($r = 0.16$, $p < 0.0001$), 6MWD ($r=-0.16$, $p < 0.0001$), BODE index ($r = 0.10$, $p < 0.005$), fibrinogen, IL6, IL8, CCL18, and SPD but not with emphysema. These variables showed significant higher values in the patients in the highest pDES quartile. pDES was elevated in patients with very high CACS in comparison with patients with lower CACS (**Figure 1**) and in patients that died during a 3 year follow-up ($p < 0.0001$).

Conclusion pDES relates to lung function, systemic inflammation, cardiovascular comorbidities, and CACS in patients with COPD. pDES is a predictor of all cause overall mortality.

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How does clinical respiratory physiology help the clinician?

S52 IS A RAISED BICARBONATE, WITHOUT HYPERCAPNIA, PART OF THE PHYSIOLOGICAL SPECTRUM OF OBESITY-RELATED HYPOVENTILATION?

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Introduction Obesity Hypoventilation Syndrome (OHS) is conventionally defined by the combination of obesity (BMI >30 kg/m^2) and daytime hypercapnia ($PaCO_2$ >6 kPa, with no other explanation) and sleep-disordered breathing may or may not be included. OHS patients have a higher morbidity, mortality, and health care utilisation compared with non-hypercapnic obese subjects. We hypothesised that in obese patients, even in the absence of a raised daytime $PaCO_2$, the presence of a raised plasma standard bicarbonate, or base excess (BE, as a biomarker of whole body acid-base balance) would be associated with some well-recognised features of OHS (reduced ventilatory drives to hypoxia and hypercapnia, and nocturnal hypoventilation), thus suggesting they represent 'early' OHS.

Abstract S52 Table 1

Mean and SDs. Ventilatory data averaged over last 5 minutes of each 15 minute challenge	Group 1 Normal $PaCO_2$ and Normal BE (n = 33)	Group 2 Normal $PaCO_2$ and Elevated BE (n = 22)	Group 3 Elevated $PaCO_2$ (OHS) (n = 16)	ANOVA p-value
BMI (kg/m^2)	45.2(9.1)	46.5(7.9)	51.6(11.7)	0.056
$PaCO_2$ (kPa)	5.15(0.47)[a]	5.42(0.32)[a]	6.62(0.91)[b]	<0.001
Base excess (mmol/l)	+0.12(1.38)[a]	+3.01(0.98)[b]	+4.78(2.10)[c]	<0.001
Hypoxic Ventilatory Response Test				
Decrease in $\%SpO_2$	2.50 (1.64)[a]	3.68 (2.07)[b]	5.01 (0.40)[b]	**0.002**
Ventilatory response (l/min/$\%SpO_2$)	2.42(4.48)	0.40(0.41)	0.66(1.20)	0.058
Hypercapnic Ventilatory Response Test				
Rise in end-tidal CO_2 (kPa)	0.73(0.33)	0.65(0.39)	0.80(0.46)	0.14
Ventilatory response to CO_2 (l/min/kPa)	1.57(0.91)	0.87(0.69)	0.70(0.59)	0.50
Sleep Data				
=4% oxygen desaturation index (ODI, events/h)	40.6(26.3)	53.9(44.5)	55.7(40.8)	0.28
Percentage of time spent with $\%SpO_2$<90%	17.3 (19.3)[a]	27.7(28.7)[b]	42.3(34.7)[b]	**0.012**

[a, b, c] grouping of data determined by ANOVA and Duncan's post hoc comparison.

Methods Obese subjects (BMI >30 kgs/m^2) were identified from a variety of sources, and divided into those with: 1) normal arterial blood gases and normal acid-base balance, 2) an isolated raised arterial BE (≥2 mmol/L), and 3) awake arterial hypercapnia (>6 kPa, i.e. established OHS). Two-point ventilatory responses to hypoxia (15 min poikilocapnic response to 15% O_2) and hypercapnia (15 min response to 5%CO_2 in O_2) were performed. Derivatives included the fall in SaO_2 and rise in end-tidal CO_2 when stable, and conventional ventilatory drive calculations. Polygraphic sleep studies were done with the derivatives of intermittent (oxygen desaturation index) and prolonged hypoxia (time below 90% SaO_2) reported here.

Results 71 subjects (BMI 47.2, SD 9.8; age 52.1, SD 8.8) were recruited into the above three groups (33, 22, and 16 respectively). The table shows the BMI, $PaCO_2$ and BE for the three groups, along with the selected derivatives of the ventilatory drive measurements and sleep studies. For nearly all the ventilatory response and sleep study derivatives, group 2 (with only an isolated raised BE) represented a middling group, and for some of the measures this middle group was more similar to group 3, with established OHS, rather than group 1.

Conclusion This study shows that obese individuals with raised BE, but without awake hypercapnia, probably represent an intermediary stage towards overt obesity-hypoventilation syndrome. Further studies will be required to establish if early intervention for this group is beneficial.

S53 NEURAL RESPIRATORY DRIVE AND SYMPTOMS LIMITING EXERCISE CAPACITY IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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